Organ and Fetal Absorbed Dose Estimates from ^{99m}Tc-Sulfur Colloid Lymphoscintigraphy and Sentinel Node Localization in Breast Cancer Patients

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The purpose of this retrospective study was to determine whether lymphoscintigraphy (LSG) for sentinel lymph node (SNL) mapping in a woman with a breast mass presents an unacceptable risk to her fetus. We assessed radiation-absorbed dose to various organs from ^{99m}Tc-sulfur colloid (TSC) LSG using standard internal absorbed dose assessment methodologies for both reference phantoms as well as for phantom models using the specific patient population characteristics such as total body and injected organ mass. The study also projected the radiation-absorbed dose to the fetus from LSG for SLN mapping. **Methods:** Data from 1,021 nonpregnant women with early-stage breast cancer who underwent SLN mapping and biopsy procedures were analyzed. Patients had a single-site intradermal injection of unfiltered TSC in 0.05 mL normal saline: 3.7 MBq (0.1 mCi) on the morning of surgery (1-d protocol) or 18.5 MBq (0.5 mCi) on the afternoon before surgery (2-d protocol). A standard internal dose calculation methodology was used to calculate absorbed doses to various organs and to a modeled fetus at 3-, 6-, and 9-mo gestation from the injection site as well as from systemic activity. **Results:** The highest estimated absorbed doses were observed for the reference 9-mo-pregnant model under the 2-d protocol. Absorbed doses of 14.9, 0.214, 0.062, 0.151, 0.004, 0.163, 0.075, and 0.014 mGy were received by the injected breast, heart, liver, lung, ovaries, thymus, total body, and fetus, respectively. Effective doses from the 2-d protocol were estimated to be 0.460, 0.186, and 0.245 mSv for the reference population, the total Memorial Sloan-Kettering Cancer Center (MSKCC) study patient population, and childbearing-age MSKCC patient population (i.e., <45 y old), respectively. **Conclusion:** SLN procedures lead to a negligible dose to the fetus of 0.014 mGy or less. This is much less than the National Council on Radiation Protection and Measurements limit to a pregnant woman. Calculations using actual patient population characteristics resulted in lower organ dose estimates than more conservative reference models.

Key Words: breast cancer; lymphoscintigraphy; sentinel lymph node mapping; absorbed dose

J Nucl Med 2006; 47:1202–1208

The sentinel lymph node (SLN) technique has proven useful for patients with melanoma (*1*) and for those with early-stage breast cancer (*2*) in guiding nodal dissections. In those with negative sentinel node evaluation, wide nodal dissections can be avoided, and the morbidity associated with a conventional lymph node dissection can be limited (*3*). In breast cancer, the SLN has been identified using blue dye (*4*), lymphoscintigraphy (LSG) with a radiocolloid such as ^{99m}Tc-sulfur colloid (TSC) (*5*), or a combination of both methods (*2*). An emerging international consensus (*6,7*), and our own experience (*3,8*), supports the use of the combined method. Moreover, SLN biopsy has essentially become the standard of care regardless of pending prospective data (*9*).

Currently we are not aware of published studies formally assessing radiation-absorbed dose to various organs from LSG for SLN mapping in breast cancer using standard, Food and Drug Administration (FDA)-reviewed absorbed dose assessment methodologies (*10*) both for both reference (or standard model) phantoms as well as for patient population phantoms, representing the median patient characteristics from a large retrospective database on sentinel node biopsy procedures using TSC.

Internal absorbed dose assessment depends on the use of mathematic formulas for absorbed dose calculation and models of the human body and its organs (*11*). The MIRD system for calculating the absorbed radiation dose resulting from a radiopharmaceutical administration (*12*) was recently

Received Feb. 6, 2006; revision accepted Mar. 20, 2006.
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updated and extended under the Organ Level Internal Dose Assessment (OLINDA; Vanderbilt University) methodology (*13*). This internal dose calculation schema has received premarket certification or 510(K) clearance from the FDA (*10*). The code specifies anthropomorphic human models, including standard reference phantoms for the adult female—both nonpregnant and at 3 stages of pregnancy: 3, 6, and 9 mo (*14*)—that were suitable for analysis of data.

The OLINDA methodology also allows for the modification of standard reference phantoms to more closely represent patient-specific factors—for example, patient weight. We used the standard anthropomorphic models as well as models modified to represent our median patient population (i.e., modified to represent median patient weight and median patient breast mass) and the median patient population of childbearing age defined for this study as women under age of 45 y.

The estimated pregnancy rate for U.S. women is 103.7 pregnancies per 1,000 women aged 15−44 y (*15*). Breast cancer is the most common malignancy associated with pregnancy, with a range of about 1 in 10,000 to 1 in 3,000 pregnancies complicated by breast cancer, resulting in an annual incidence of ~3,500 cases of breast cancer in pregnancy in the United States (*16*). It is expected that with an increasing trend toward delayed childbearing, breast malignancies diagnosed during pregnancy may become more common (*17,18*).

SLN biopsy procedures using radioactive TSC have historically been contraindicated for pregnant breast cancer patients (*19,20*) because of the assumed risk of radiation exposure. However, there is no concrete evidence or published data that have demonstrated significant risk from exposure. No studies are reported in the literature of internal radiation-absorbed dose assessment using standard methodologies for absorbed dose to the fetus from lymphoscintigraphy (*21*). A prior study using thermoluminescent dosimeters placed on the patient's abdomen to evaluate external exposure estimated that the fetal dose was nonhazardous (*22*). This study was undertaken to assess the radiation-absorbed dose to the fetus using phantom-based internal dosimetric estimation and, thereby, to evaluate the relationship between risks and benefits of this procedure in this radiosensitive population.

MATERIALS AND METHODS

Study Population

A retrospective analysis of data of 1,021 women with breast cancer who underwent LSG, SLN mapping, and biopsy procedures on a single breast from January 2000 through April 2001 was performed. All patients studied had their procedure at the same location, Memorial Sloan-Kettering Cancer Center (MSKCC). The retrospective study was approved by the MSKCC institutional review board. Informed consent for this analysis was not judged necessary as all patient identifiers were removed from the database and the dataset was managed in accordance with Health Insurance Portability and Accountability Act (HIPAA) regulations.

Clinical Lymphoscintigraphic Techniques for Breast Cancer

All patients had a single intradermal injection of unfiltered TSC (CIS-US), administered by an experienced nuclear medicine physician or nurse. The radiopharmaceutical was prepared to ensure quality control and consistent particle size (*3*). The tracer was injected directly over the palpable tumor or just cephalad to the scar in those who had prior surgical or excisional biopsy.

Two scanning techniques were used to identify SLNs. In those patients where sentinel node mapping was done on the same day before surgery (1-d protocol), 3.7 MBq (0.1 mCi) of TSC in a 0.05-mL volume with saline were injected, followed by imaging. In other patients, injection of tracer and scanning was done on the day before surgery (2-d protocol). For this protocol, 18.5 MBq (0.5 mCi) of TSC in a 0.05-mL volume were injected.

Anterior and lateral images of the chest including the axilla were obtained at 20−30 min after injection in the 1-d protocol and at ~2 h after injection for the 2-d protocol patients. A transmission ^{57}Co flood source was used to silhouette the patient during the 5-min image acquisition, allowing localization of the SLN (*3*) (Fig. 1). Surgery was usually performed within 4 h after injection (1-d protocol) or early the following morning (2-d protocol). SLN biopsy procedures were similar to those described previously (*3,8*).

Internal Radiation-Absorbed Dose Assessment

Absorbed doses were estimated for the uterus, fetus, placenta, and various other organs. In addition, the effective dose (*23*) to the whole body of the pregnant and nonpregnant models were estimated in this present study.

In performing absorbed dose calculations, 2 pathways were considered. First, the direct absorbed dose from the breast as a source of TSC to various organs was determined (breast-as-source pathway). Second, an estimate of the absorbed dose from systemic TSC in the blood to various organs was determined (total body-as-source pathway). These pathways were summed to arrive at a total absorbed dose estimate for the reference models and the study patient populations for the 1-d and 2-d protocols. In addition, the effective dose was calculated to represent the dose resulting from an equivalent exposure from a uniform irradiation of the whole body. This is a useful parameter for comparing "whole-body equivalent" doses for various radiopharmaceutical and diagnostic procedures.

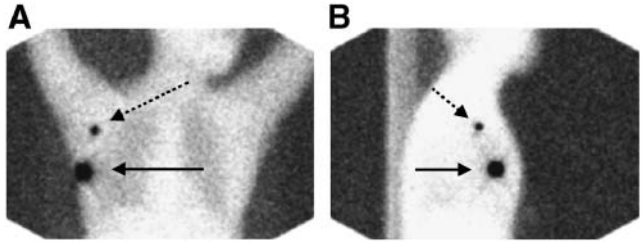

FIGURE 1. Anterior (A) and right lateral (B) transmission images obtained 30 min after lymphoscintigraphic injection in left breast show injection site (solid arrow) and focal uptake (dashed arrow) in sentinel node in right axilla.

TABLE 1
Doses (mGy/MBq) from Combined Sources (Injected Breast + Total Body) to Adult Nonpregnant Female Models

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	1.95E−03	1.76E−03	1.83E−03
Brain	1.50E−04	1.35E−04	1.40E−04
Injected breast	8.04E−01	2.97E−01	4.04E−01
Gallbladder wall	1.46E−03	1.32E−03	1.36E−03
LLI wall	1.80E−04	1.62E−04	1.68E−04
Small intestine	3.69E−04	3.33E−04	3.45E−04
Stomach wall	2.55E−03	2.31E−03	2.40E−03
ULI wall	5.38E−04	4.87E−04	5.05E−04
Heart wall	1.05E−02	9.49E−03	9.84E−03
Kidneys	8.30E−04	7.51E−04	7.79E−04
Liver	2.83E−03	2.56E−03	2.66E−03
Lungs	7.90E−03	7.16E−03	7.42E−03
Muscle	1.74E−03	1.57E−03	1.63E−03
Ovaries	1.79E−04	1.62E−04	1.68E−04
Pancreas	2.41E−03	2.18E−03	2.26E−03
Red marrow	1.90E−03	1.71E−03	1.78E−03
Osteogenic cells	3.11E−03	2.81E−03	2.91E−03
Skin	2.82E−03	2.56E−03	2.65E−03
Spleen	1.67E−03	1.51E−03	1.57E−03
Thymus	9.99E−03	9.05E−03	9.38E−03
Thyroid	1.27E−03	1.15E−03	1.20E−03
Bladder wall	1.46E−04	1.32E−04	1.37E−04
Uterus	1.88E−04	1.70E−04	1.77E−04
Fetus	0.00E+00	0.00E+00	0.00E+00
Placenta	0.00E+00	0.00E+00	0.00E+00
Total body	4.11E−03	3.67E−03	3.83E−03
Effective dose (mSv/MBq)	2.47E−02	9.90E−03	1.31E−02

TABLE 2
Doses (mGy/MBq) from Combined Sources (Injected Breast + Total Body) to 3-Month-Pregnant Models

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	1.94E−03	1.76E−03	1.83E−03
Brain	1.50E−04	1.35E−04	1.41E−04
Injected breast	8.04E−01	2.97E−01	4.04E−01
Gallbladder wall	1.45E−03	1.32E−03	1.36E−03
LLI wall	1.73E−04	1.55E−04	1.62E−04
Small intestine	4.14E−04	3.75E−04	3.89E−04
Stomach wall	2.54E−03	2.30E−03	2.39E−03
ULI wall	5.27E−04	4.78E−04	4.96E−04
Heart wall	1.05E−02	9.49E−03	9.84E−03
Kidneys	8.28E−04	7.50E−04	7.77E−04
Liver	2.83E−03	2.56E−03	2.66E−03
Lungs	7.90E−03	7.16E−03	7.42E−03
Muscle	1.74E−03	1.57E−03	1.63E−03
Ovaries	1.71E−04	1.55E−04	1.60E−04
Pancreas	2.41E−03	2.18E−03	2.26E−03
Red marrow	1.90E−03	1.71E−03	1.78E−03
Osteogenic cells	3.11E−03	2.81E−03	2.91E−03
Skin	2.82E−03	2.56E−03	2.65E−03
Spleen	1.67E−03	1.51E−03	1.56E−03
Thymus	9.99E−03	9.05E−03	9.38E−03
Thyroid	1.27E−03	1.15E−03	1.20E−03
Bladder wall	1.21E−04	1.09E−04	1.13E−04
Uterus	1.76E−04	1.59E−04	1.65E−04
Fetus	2.06E−04	1.85E−04	1.92E−04
Placenta	0.00E+00	0.00E+00	0.00E+00
Total body	4.11E−03	3.67E−03	3.83E−03
Effective dose (mSv/MBq)	2.47E−02	9.90E−03	1.30E−02

For the breast-as-source pathway, it was assumed that the activity in the injection site remained localized at the site and sentinel node until complete decay of the ^{99m}Tc (i.e., using a physical half-life of 6.01 h), even though some patients with total mastectomy may not have residual tissue retaining all of the activity. This assumption is consistent with the literature (*24,25*). For the total body-as-source pathway we assumed that 1% of the injected activity is distributed in the blood volume (*22,24*) until complete decay. Direct doses to the injected breast were estimated by calculating the doses from TSC to spheric masses using the OLINDA methodology and conservatively assuming that all of the TSC is retained as a localized activity source within the tissue of the breast and that it completely decays with the physical half-life.

RESULTS

Study Population Statistics

One thousand twenty-one women underwent SLN mapping and biopsy using intradermal injections of TSC. The average patient weight was 69.3 ± 15.6 kg (mean ± SD), with a median weight of 66 kg. The average age was 56.4 ± 12.7 y, with a median age of 56 y; 21.4% of patients were ≤45 y of age and 11.3% were ≤40 y of age. For the database population of childbearing age, 219 women, the average age was 39.5 ± 4.5 y, with a median age of 40 y.

Seven hundred eighteen (70.2%) of the women underwent lumpectomy, wherein the TSC injection site remained intact after the surgery. One hundred seventy-seven (17.3%) of the women underwent tissue-conserving mastectomy, wherein the TSC injection site remained intact after the surgery. One hundred twenty-eight women (12.5%) underwent full mastectomies, wherein the TSC injection site (tissue and skin) was removed during the surgery. The median time from injection to the end of the surgery was 1,316 min for the 18.5-MBq (2 d) protocol and 275 min for the 3.7-MBq (1 d) protocol. In 39 patients, the mass of the single removed breast tissue ranged from 210 to 2,000 g, with an average of 613 ± 380 g and a median mass of 550 g.

For a subset of 5 cases in the childbearing population, the mass of the removed single breast tissue ranged from 151 to 600 g, with an average of 375.4 ± 165 g and a median mass of 390 g.

Organ Dose Estimates

The doses per unit injected activity (mGy/MBq) from the combined sources (i.e., injected breast-as-source plus the total body-as-source), to various organs, and the effective

TABLE 3
Doses (mGy/MBq) from Combined Sources (Injected Breast + Total Body) to 6-Month-Pregnant Models

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	1.94E−03	1.76E−03	1.83E−03
Brain	1.46E−04	1.31E−04	1.36E−04
Injected breast	8.04E−01	2.97E−01	4.04E−01
Gallbladder wall	1.59E−03	1.44E−03	1.49E−03
LLI wall	4.12E−04	3.74E−04	3.88E−04
Small intestine	6.08E−04	5.49E−04	5.71E−04
Stomach wall	3.19E−03	2.88E−03	2.99E−03
ULI wall	1.63E−03	1.47E−03	1.53E−03
Heart wall	1.16E−02	1.05E−02	1.09E−02
Kidneys	8.27E−04	7.49E−04	7.76E−04
Liver	3.35E−03	3.03E−03	3.15E−03
Lungs	8.17E−03	7.40E−03	7.68E−03
Muscle	1.75E−03	1.58E−03	1.64E−03
Ovaries	1.95E−04	1.77E−04	1.83E−04
Pancreas	2.41E−03	2.18E−03	2.26E−03
Red marrow	1.90E−03	1.71E−03	1.78E−03
Osteogenic cells	3.10E−03	2.80E−03	2.91E−03
Skin	2.92E−03	2.65E−03	2.75E−03
Spleen	1.67E−03	1.51E−03	1.56E−03
Thymus	8.83E−03	8.00E−03	8.29E−03
Thyroid	1.27E−03	1.15E−03	1.19E−03
Bladder wall	1.34E−04	1.21E−04	1.26E−04
Uterus	6.86E−04	6.20E−04	6.44E−04
Fetus	6.18E−04	5.59E−04	5.81E−04
Placenta	1.30E−03	1.18E−03	1.22E−03
Total body	3.99E−03	3.56E−03	3.71E−03
Effective dose (mSv/MBq)	2.49E−02	1.01E−02	1.32E−02

TABLE 4
Doses (mGy/MBq) from Combined Sources (Injected Breast + Total Body) to 9-Month-Pregnant Models

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	1.94E−03	1.76E−03	1.83E−03
Brain	1.46E−04	1.32E−04	1.37E−04
Injected breast	8.04E−01	2.97E−01	4.04E−01
Gallbladder wall	1.58E−03	1.43E−03	1.49E−03
LLI wall	3.18E−04	2.88E−04	2.99E−04
Small intestine	1.89E−03	1.71E−03	1.78E−03
Stomach wall	3.19E−03	2.88E−03	2.99E−03
ULI wall	1.82E−03	1.65E−03	1.71E−03
Heart wall	1.16E−02	1.05E−02	1.09E−02
Kidneys	8.26E−04	7.48E−04	7.75E−04
Liver	3.35E−03	3.03E−03	3.15E−03
Lungs	8.17E−03	7.40E−03	7.68E−03
Muscle	1.80E−03	1.62E−03	1.68E−03
Ovaries	1.96E−04	1.77E−04	1.83E−04
Pancreas	2.40E−03	2.18E−03	2.26E−03
Red marrow	1.90E−03	1.71E−03	1.78E−03
Osteogenic cells	3.10E−03	2.80E−03	2.91E−03
Skin	2.98E−03	2.70E−03	2.80E−03
Spleen	1.67E−03	1.51E−03	1.56E−03
Thymus	8.83E−03	8.00E−03	8.29E−03
Thyroid	1.27E−03	1.15E−03	1.19E−03
Bladder wall	1.25E−04	1.13E−04	1.17E−04
Uterus	8.63E−04	7.81E−04	8.10E−04
Fetus	7.39E−04	6.69E−04	6.94E−04
Placenta	1.58E−03	1.44E−03	1.49E−03
Total body	4.04E−03	3.61E−03	3.77E−03
Effective dose (mSv/MBq)	2.49E−02	1.00E−02	1.32E−02

dose for the OLINDA reference adult female, the MSKCC patient population, and the MSKCC patient population of childbearing age are listed in Table 1. Similarly, the doses to 3-, 6-, and 9-mo-pregnant populations are listed in Tables 2, 3, and 4, respectively. The breast-as-source pathway resulted in much higher dose estimates than the total body-as-source (i.e., the blood pathway). The injected breast-as-source pathway represented >95% of the estimated organ doses for all organs in all models with the exception of the following organs in which the breast-as-source pathway represented >65% of the estimated organ doses: urinary bladder wall, brain, ovaries, lower large intestine wall, and kidneys (see Table 5 for breast-as-source fractions for the 9-mo-pregnant populations).

Highest estimated doses to organs and fetus are seen for the 9-mo-pregnant populations. Table 6 lists the estimated organ doses from the 1-d protocol. Table 7 lists the estimated organ doses from the 18.5-MBq 2-d protocol. Highest dose estimates are seen for the reference model population. Effective doses were lowest in the MSKCC patient population. Total doses to the injected breast ranged from 5.49 mGy (0.55 rad) to 14.9 mGy (1.5 rad) for the 2-d protocol.

Organ and effective dose estimates obtained from this study are consistent with literature estimates. Zanzonico (*26*) collated data from several references. Table 8 compares the dose estimates from this study with the literature reported estimates and shows excellent agreement with doses to the injected breast, heart wall, liver, lungs, ovaries (gonads), thymus, and total body.

Our results were generated using the conservative assumption that the injection site and total-body activity remains with the patient until all of the radioactive material completely decays. Patients that have the injection site removed would have the dose estimate further reduced. For these cases, the cumulated activity and, hence, the dose estimates would be reduced to a factor of approximately 40% and 90% of the conservative assumption estimates for the 1- and 2-d protocols, respectively.

DISCUSSION

Using the reference models and conservative assumptions, the overall maximum estimated dose to the fetus is to the 9-mo-fetal model: 1.37E−02 mGy (1.37E−03 rad) for the combined breast-as-source and total body-as-source pathways for the 2-d protocol. This value is

TABLE 5
Fraction of Combined Doses from Injected Breast

Organ	Fraction
Bladder wall	0.65
Brain	0.70
Ovaries	0.70
LLI wall	0.84
Kidneys	0.93
Fetus	0.95
Uterus	0.95
Osteogenic cells	0.95
Thyroid	0.96
Gallbladder wall	0.96
Spleen	0.97
Adrenals	0.97
Small intestine	0.97
Pancreas	0.97
Red marrow	0.97
Muscle	0.97
ULI wall	0.98
Placenta	0.98
Liver	0.98
Stomach wall	0.98
Total body	0.99
Skin	0.99
Lungs	0.99
Thymus	0.99
Heart wall	0.99
Injected breast	1.00

TABLE 6
Doses (mSv) to 9-Month-Pregnant Models from 3.7-MBq 1-Day Protocol

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	7.19E−03	6.50E−03	6.76E−03
Brain	5.39E−04	4.87E−04	5.06E−04
Injected breast	2.97E+00	1.10E+00	1.49E+00
Gallbladder wall	5.84E−03	5.30E−03	5.49E−03
LLI wall	1.18E−03	1.07E−03	1.11E−03
Small intestine	6.99E−03	6.34E−03	6.57E−03
Stomach wall	1.18E−02	1.07E−02	1.11E−02
ULI wall	6.73E−03	6.09E−03	6.32E−03
Heart wall	4.28E−02	3.87E−02	4.02E−02
Kidneys	3.05E−03	2.77E−03	2.87E−03
Liver	1.24E−02	1.12E−02	1.16E−02
Lungs	3.02E−02	2.74E−02	2.84E−02
Muscle	6.64E−03	6.00E−03	6.23E−03
Ovaries	7.25E−04	6.55E−04	6.77E−04
Pancreas	8.90E−03	8.06E−03	8.36E−03
Red marrow	7.03E−03	6.34E−03	6.57E−03
Osteogenic cells	1.15E−02	1.04E−02	1.08E−02
Skin	1.10E−02	9.99E−03	1.04E−02
Spleen	6.17E−03	5.60E−03	5.79E−03
Thymus	3.27E−02	2.96E−02	3.07E−02
Thyroid	4.69E−03	4.27E−03	4.42E−03
Bladder wall	4.62E−04	4.17E−04	4.33E−04
Uterus	3.19E−03	2.89E−03	3.00E−03
Fetus	2.73E−03	2.48E−03	2.57E−03
Placenta	5.85E−03	5.32E−03	5.51E−03
Total body	1.49E−02	1.34E−02	1.39E−02
Effective dose	9.19E−02	3.72E−02	4.90E−02

consistent with the fetal dose estimates of Keleher et al. (*21*), who estimated a dose of 7.74E−2 mGy/92.5 MBq to the 9-mo fetus under assumptions that used the heart as a surrogate for a single breast injection. Their estimate translates to about 1.55E−2 mGy/18.5 MBq and is essentially equal to our fetal estimates. Our estimated value is also comparable with reported estimates for the gonads and liver of an adult female undergoing SLN detection with 18.5-MBq TSC (*26*); the range of effective doses estimated in this article of 1.86E−01 to 4.60E−01 mGy (1.86E−02 to 4.60E−02 rad) are similar to the value of 3.2E−01 mSv (3.2E−2 rem) reported elsewhere in the literature (*24*). We, therefore, believe our estimates of doses to the fetus to be reasonably accurate and represent the best estimates of such doses for both the reference models and the MSKCC patient population on the basis of the assumptions and models used.

For our study, the assumption of 1% of injected activity to the blood is considered conservative because of the large-size colloid used. Assuming that 5% of the injected activity goes to the blood (presumably from a smaller colloid size), the maximum fetal dose would be estimated at 0.0165 mGy (as compared with the 0.0137 mGy for the 1% model). The potential doses from the fetus from the small amount of activity excreted through the urinary bladder are considered negligible (*27*) and under the conservative assumption that all blood activity reaches the urinary bladder would be <0.002 mGy for the 2-d protocol. In addition, there is negligible additional dose from the flood source with ~0.2 μGy.

The fact sheet for physicians on prenatal radiation exposures by the Centers for Disease Control and Prevention notes that, at <50 mSv (5 rem) delivered at any time after conception, noncancer health effects are not detectable and that the estimated increased risk of childhood cancer is 0%−1% (*28*). Brent (*29*) discusses the effects of intrauterine radiation exposure and notes that almost all of the effects of intrauterine radiation are deterministic, suggesting that exposures of <0.05 Gy represent nonmeasurable reproductive risks and are well below the 0.2-Gy threshold for congenital malformations, growth retardation, neurodevelopmental abnormalities, and other reproductive effects. Timins (*30*) also reported that doses of <100 mGy do not increase the risk of fetal malformation. The International Commission on Radiation Protection (ICRP) similarly noted that the risk to the fetus can be considered negligible for low-dose procedures (i.e., <1 mSv during the pregnancy) and they further emphasize that termination of pregnancy at fetal doses of <100 mGy (10,000 mrad) is not justified on the basis of radiation risk (*31*).

TABLE 7
Doses (mSv) to 9-Month-Pregnant Models from 18.5-MBq 2-Day Protocol

Organ	Reference model	MSKCC model	MSKCC childbearing model
Adrenals	3.59E−02	3.25E−02	3.38E−02
Brain	2.70E−03	2.44E−03	2.53E−03
Injected breast	1.49E+01	5.49E+00	7.47E+00
Gallbladder wall	2.92E−02	2.65E−02	2.75E−02
LLI wall	5.89E−03	5.33E−03	5.53E−03
Small intestine	3.50E−02	3.17E−02	3.28E−02
Stomach wall	5.89E−02	5.33E−02	5.53E−02
ULI wall	3.37E−02	3.04E−02	3.16E−02
Heart wall	2.14E−01	1.93E−01	2.01E−01
Kidneys	1.53E−02	1.38E−02	1.43E−02
Liver	6.20E−02	5.61E−02	5.82E−02
Lungs	1.51E−01	1.37E−01	1.42E−01
Muscle	3.32E−02	3.00E−02	3.11E−02
Ovaries	3.63E−03	3.27E−03	3.39E−03
Pancreas	4.45E−02	4.03E−02	4.18E−02
Red marrow	3.51E−02	3.17E−02	3.28E−02
Osteogenic cells	5.74E−02	5.18E−02	5.38E−02
Skin	5.52E−02	4.99E−02	5.18E−02
Spleen	3.09E−02	2.80E−02	2.89E−02
Thymus	1.63E−01	1.48E−01	1.53E−01
Thyroid	2.35E−02	2.13E−02	2.21E−02
Bladder wall	2.31E−03	2.08E−03	2.16E−03
Uterus	1.60E−02	1.44E−02	1.50E−02
Fetus	1.37E−02	1.24E−02	1.28E−02
Placenta	2.93E−02	2.66E−02	2.75E−02
Total body	7.47E−02	6.69E−02	6.97E−02
Effective dose	4.60E−01	1.86E−01	2.45E−01

Deterministic effects such as neurologic impairment in offspring have not been seen for doses of <100 mGy (*32*). The National Council on Radiation Protection (NCRP) (*33*) states that even for a highly unlikely 50-mSv dose to a pregnant woman, the risk is small compared with other risks to the fetus (*34*). For the purposes of radiation protection, the NCRP (*32*) suggests using a nonthreshold linear dose–response model and, therefore, recommends a dose limit to pregnant women of 1 mSv/y (*35*).

Rather than perform an internal dose assessment as in this current study, Gentilini et al. (*22*) performed a study using thermoluminescent dosimetry measurements of skin surface dose as a surrogate for fetal and uterine dose estimates and they concluded that lymphoscintigraphy and sentinel node biopsy can be performed safely during pregnancy. Similarly, Richards and Stasko (*36*) note that TSC provides negligible ionizing radiation to the fetus during the SLN procedure for melanoma in a pregnant patient. In addition, Nicklas and Baker (*37*) suggest that the SLN procedure can be safety performed in pregnancy, with negligible risk to the fetus, because the entire radioisotope stays trapped at the site of injection or within the lymphatics until decay occurs, and the exposure to the fetus is essentially zero.

When compared with the limits and risks, our estimates on maximum fetal doses are negligible and are well below levels associated with risk concerns. Under "worst-case" conservative assumptions, the maximum estimated fetal exposures reported here (for the 18.7-MBq 2-d protocol) are <3% of the Nuclear Regulatory Commission (NRC) monthly guideline of 0.5 mSv and <0.3% of the NRC occupational exposure limits during the gestation period of 5 mSv. In fact, the maximum estimated fetal doses are equivalent to the dose received by the mother from about 1 d of natural background radiation in the United States. Estimated doses for the SLN procedure in carcinoma of the breast can be compared with several commonly performed nuclear medicine and radiographic procedures (*38–40*), showing much less dose from SLN. When compared with the dose resulting from several natural and man-made sources (*38,39*), including the average annual effective dose equivalent to a member of the U.S. population of ~3.6 mSv, the estimated doses from SLN are very low.

CONCLUSION

Characteristics of a real patient population can be identified from patient data for more accurately estimating organ absorbed doses. Considering actual patient population characteristics resulted in lower organ dose estimates than conservative reference models. Estimated fetal dose was negligible and is much less than the NCRP limit of 1 mSv over the gestation period for a declared pregnant woman. Therefore, using our standard techniques, LSC with TSC for SLN mapping can be safely applied during pregnancy, as estimated fetal doses are not associated with significantly increased risk to the fetus.

TABLE 8
Comparison of Estimated Doses (mSv) to 9-Month-Pregnant Models from 18.5-MBq (0.5 mCi) 2-Day Protocol with Literature Estimates

Organ	Reference model	MSKCC model	MSKCC childbearing model	Zanzonico (*26*)
Injected breast	1.49E+01	5.49E+00	7.47E+00	1.10E+01
Heart wall	2.14E−01	1.93E−01	2.01E−01	3.20E−01
Liver	6.20E−02	5.61E−02	5.82E−02	1.60E−02 to 2.40E−01
Lungs	1.51E−01	1.37E−01	1.42E−01	1.20E−01
Ovaries	3.63E−03	3.27E−03	3.39E−03	~0 to 8.90E−02
Thymus	1.63E−01	1.48E−01	1.53E−01	1.50E−01
Total body	7.47E−02	6.69E−02	6.97E−02	8.10E−03 to 7.3E−02

REFERENCES

1. Morton DL, Wen DR, Wong JH, et al. Technical details of intraoperative lymphatic mapping for early stage melanoma. *Arch Surg.* 1992;127:392–399.
2. Albertini JJ, Lyman GH, Cox C, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA.* 1996;276:1818–1822.
3. Yeung HW, Cody IH, Turlakow A, et al. Lymphoscintigraphy and sentinel node localization in breast cancer patients: a comparison between 1-day and 2-day protocols. *J Nucl Med.* 2001;42:420–423.
4. Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg.* 1994;220:391–398.
5. Krag DN, Weaver DL, Alex JC, Fairbank JT. Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe. *Surg Oncol.* 1993;2:335–339.
6. Goyal A, Newcombe RG, Mansel RE, et al. Role of routine preoperative lymphoscintigraphy in sentinel node biopsy for breast cancer. ALMANAC Trialists Group. *Eur J Cancer.* 2005;41:238–243.
7. Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer: a multicenter validation study. *N Engl J Med.* 1998;339:941–946.
8. Hill AD, Tran KN, Akhurst T, et al. Lessons learned from 500 cases of lymphatic mapping for breast cancer. *Ann Surg.* 1999;229:528–535.
9. Hampton T. Surgeons "vote with their feet" for sentinel node biopsy for breast cancer staging. *JAMA.* 2003;290:3053–3054.
10. Stabin MG. OLINDA/EXM Personal Computer Code. Available at: http://www.doseinfo-radar.com/OLINDA.html. Accessed: May 24, 2006.
11. Stabin MG, Siegel JA. Physical models and dose factors for use in internal dose assessment. *Health Phys.* 2003;85:294–310.
12. Loevinger R, Budinger TF, Watson EE. *MIRD Primer for Absorbed Dose Calculations.* New York, NY: Society of Nuclear Medicine; 1991.
13. Stabin MG. *OLINDA 1.0 Documentation Package.* Nashville, TN: Vanderbilt University; 2004.
14. Stabin MG, Watson EE, Cristy M, et al. Mathematical models and specific absorbed fractions of photon energy in the nonpregnant adult female and at the end of each trimester of pregnancy. ORNL Report ORNL/TM-12907. Oak Ridge, TN: Oak Ridge National Laboratory; 1995.
15. Ventura SJ, Mosher WD, Curtin SC, Abma JC, Henshaw S. Trends in pregnancy rates for the United States, 1976−1997: an update. *Natl Vital Stat Rep.* 2001;49:1–9.
16. Moore HC, Foster RS Jr. Breast cancer and pregnancy. *Semin Oncol.* 2000;27:646–653.
17. Berry DL, Theriault RL, Holmes FA, et al. Management of breast cancer during pregnancy using a standardized protocol. *J Clin Oncol.* 1999;17:855–861.
18. Puckridge PJ, Saunders CM, Ives AD, Semmens JB. Breast cancer and pregnancy: a diagnostic and management dilemma. *ANZ J Surg.* 2003;73:500–503.
19. Woo JC, Yu T, Hurd TC. Breast cancer in pregnancy: a literature review. *Arch Surg.* 2003;138:91–98.
20. Schwartz GF, Giuliano AE, Veronesi U: Consensus Conference Committee. Proceedings of the Consensus Conference on the Role of Sentinel Lymph Node Biopsy in Carcinoma of the Breast, April 19−22, 2001, Philadelphia, Pennsylvania. *Cancer.* 2002;94:2542–2551.
21. Keleher A, Wendt R 3rd, Delpassand E, Stachowiak AM, Kuerer HM. The safety of lymphatic mapping in pregnant breast cancer patients using Tc-99m sulfur colloid. *Breast J.* 2004;10:492–495.
22. Gentilini O, Cremonesi M, Trifiro G, et al. Safety of sentinel node biopsy in pregnant patients with breast cancer. *Ann Oncol.* 2004;15:1348–1351.
23. ICRP. *1990 Recommendations of the ICRP: International Commission on Radiological Protection. Publication 60.* New York, NY: Pergamon Press; 1990.
24. Keshtgar MR, Waddington W, Lakhani SR, Ell PJ. *The Sentinel Node in Surgical Oncology.* Berlin, Germany: Springer-Verlag; 1999.
25. Strzelczyk I, Finlayson C. Sentinel node biopsy: ALARA and other considerations. *Health Phys.* 2004;86(2 suppl):S31–S34.
26. Zanzonico P. The intraoperative gamma probe: design, operation, and safety. In: Cody H, ed. *Sentinel Node Biopsy.* New York, NY: Taylor & Francis; 2001.
27. Paganelli G, Ferrari M, Cremonesi M, Gentilini O, Trifiro G. Optimised lymphoscintigraphy in pregnant patients with breast cancer is safe [reply letter]. *Ann Oncol.* 2005;16:674–675.
28. CDC. Prenatal radiation exposure: a fact sheet for physicians. Atlanta, GA: Centers for Disease Control and Prevention; 2003. Available at: http://www.bt.cdc.gov/radiation/prenatalphysician.asp. Accessed May 16, 2006.
29. Brent RL. Utilization of developmental basic science principles in the evaluation of reproductive risks from pre- and postconception environmental radiation exposures. *Teratology.* 1999;59:182–204.
30. Timins JK. Radiation during pregnancy. *N J Med.* 2001;98:29–33.
31. ICRP. Pregnancy and medical radiation. International Commission on Radiological Protection. ICRP Publication no. 84. *Ann ICRP.* 2000;30(1):1–43.
32. NCRP. *Limitation of Exposure to Ionizing Radiation. NCRP Report no. 116.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1993.
33. NCRP. *Risk Estimates for Radiation Protection. NCRP Report no. 115.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1993.
34. Nickoloff EL, Brateman L. Proposition: a pregnant resident physician should be excused from training rotations such as angiography and nuclear medicine because of the potential exposure of the fetus. *Med Phys.* 1999;26:2517–2519.
35. NCRP. *Considerations Regarding the Unintended Radiation Exposure of the Embryo, Fetus or Nursing Child: Commentary no. 9.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1994.
36. Richards KA, Stasko T. Dermatologic surgery and the pregnant patient. *Dermatol Surg.* 2002;28:248–256.
37. Nicklas AH, Baker ME. Imaging strategies in the pregnant cancer patient. *Semin Oncol.* 2000;27:623–632.
38. ICRP. *Summary of Current ICRP Report of Committee 3: Principles for Protection of Patient in Nuclear Medicine*: International Commission on Radiological Protection; 1993.
39. NCRP. *Exposure of the U.S. Population from Diagnostic Medical Radiation: Recommendations of the National Council on Radiation Protection and Measurements. NCRP Report no. 100.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1989.
40. NCRP. *Sources and Magnitude of Occupational and Public Exposures from Nuclear Medicine Procedures: Recommendations of the National Council on Radiation Protection and Measurements. NCRP Report no. 124.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1996.

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J Nucl Med. 2006;47:1202-1208.

The Journal of Nuclear Medicine is published monthly.
SNMMI | Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive, Reston, VA 20190.
(Print ISSN: 0161-5505, Online ISSN: 2159-662X)

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